

Alexithymia; an often missed condition prevalent in the practice of nephrology

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Cite this article as: Yeşil E, Pehlivan Ö, Toprak Z, Surardamar A. Alexithymia; an often missed condition prevalent in the practice of nephrology. Anatolian Curr Med J 2023; 5(1); 18-23.

ABSTRACT

Aim: Alexithymia is a disorder associated with difficulty in recognizing and expressing feelings, which can lead to an increased susceptibility to disease development that makes alexithymia a possible risk factor for chronic kidney disease (CKD). This study was performed to evaluate for alexithymia in pre-dialysis CKD and end-stage renal disease patients undergoing hemodialysis.

Material and Method: The study was conducted in the Nephrology Outpatient Department and Hemodialysis unit of Ümraniye Research and Training Hospital. The patients had to have a diagnosis of CKD. Demographic data form, routine biochemical follow up data of patients, Toronto Alexithymia Scale (TAS), and Hospital Depression and Anxiety Scale (HADS) were used in this study. The statistical significance level was determined as $p < 0.05$.

Results: A total of 111 patients (mean age 58.10 ± 13.48 years, 61% female) were included in the study, 83.9% of whom were found to have alexithymia. The incidence of alexithymia in CDK patients was significantly higher than that in the control group ($p = 0.004$); however, no statistically significant difference was detected in its incidence between the hemodialysis and pre-dialysis groups ($p > 0.05$). The results showed that increased incidence of depression resulted in a 4.47-fold ($p = 0.035$) increase in the incidence of alexithymia.

Conclusion: Alexithymia has been found to be high in patients with chronic kidney disease. Therefore, it is essential that we be aware of patients' emotional stress and assess them for depression, anxiety, and alexithymia.

Keywords: Alexithymia, chronic kidney disease, hemodialysis

INTRODUCTION

Chronic kidney disease (CKD) is defined as a state of decreased glomerular function with creatinine clearance lower than $60 \text{ mL/min/1.73 m}^2$, which is ongoing for at least 3 months. (1). Chronic hemodialysis is initiated in stage 5 CKD, when the glomerular filtration rate (GFR) is under 10 mL/min , taking other clinical indicators into account, such as presence of hypervolemia, hyperkalemia, metabolic acidosis, and patient's comorbidities (2). Prolonged inactivity, dependence on the dialysis machines, continuous medication, intensive diet, and fluid restriction cause physical and physiological pathologies in these patients (3). Alexithymia is a concept that describes the inability to differentiate between bodily sensations and emotions as well as difficulty in describing emotions. The main characteristics of this disorder are dysfunction in social attachment, emotional awareness and relationship with other people. In addition, people with

alexithymia have difficulty in appreciating the emotions of other people and they seem to be unemphatic.. Alexithymia may be neurological, which may be caused by disruptions in the neuronal pathways that process emotions, and can also develop as a self defense measure against stressful situations such as terminal illness, which is then called psychological alexithymia (4). Severe alexithymia is a predisposing factor for many psychiatric and somatic disorders (5), and studies have shown that there is a high incidence of alexithymia in patients undergoing hemodialysis (4-6). In addition, it has been shown that higher psychological distress contributes to increased comorbidity and earlier mortality in patients with CKD (7).

This study aimed to evaluate the prevalence of alexithymia and its relation with depression and anxiety in CKD patients in the predialysis stage as well as in those receiving hemodialysis.

MATERIAL AND METHOD

The study was carried out with the permission of Ümraniye Training and Research Hospital Clinical Researches Ethics Committee (Date: 21.04.2022, Decision No: B.10.1.TKH.4.34. H.GPO.0.01/156). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

A total of 111 participants, including CKD patients undergoing hemodialysis (n:72) and patients in pre-dialysis stage of CKD (n:39), were included in this study, and all were informed about data privacy and provided written informed consent. The patients who were in pre-hemodialysis stage randomly selected among those who came to the outpatient clinic within 2 months. The inclusion criterias were; 1) ability to understand and speak Turkish, 2) age between 18 and 75 years, 3) patients receiving hemodialysis for at least 3 months and patients with diagnosis of CKD and a GFR of <60 ml/min/day, 4) signed informed consent for the study. Exclusion criterias were; 1) use of anti-stress and anxiety medications 2) a diagnosis of any mental disorder. 33 subjects between the ages of 18-65 without a psychiatric or physiological disorder were included in the control group.

This study lasted for 8 weeks, during which blood samples were obtained from the pre-dialysis patients in the morning after an overnight fast of at least 12 hours. In the hemodialysis patients, blood samples were taken before and after hemodialysis, while the urea, creatinine, sodium, potassium, c-reactive protein, albumin, ferritin, and hemoglobin levels of all patients were also measured. In addition, Kt/v and URR values were noted for the hemodialysis patients. The patients' demographic data were obtained using a data collection form prepared by the researchers, requesting for patients' age, gender, duration of dialysis/disease, etiology of CKD, education status, and marital status. The patients were asked to complete two questionnaires: 1) the Toronto Alexithymia Scale (TAS-20) and 2) the Hospital Anxiety and Depression Scale (HADS). Patients undergoing hemodialysis filled out the forms during hemodialysis sessions. Patients in pre-dialysis stage forms were given to them to complete and return. Finally the patients were divided into two groups according to the development of alexithymia and the data were compared according to these groups.

The HADS is a 14-item self-report questionnaire that includes an anxiety (HADS-A) and a depression score (HADS-D) for assessing symptoms of anxiety and depression. HADS-A and HADS-D can be combined to give HADS-total, and the use of HADS has been confirmed for evaluating patients between the ages of 18 and 79 years with an appropriate average internal consistency for the depression (Cronbach's $\alpha=.75$) and

anxiety (Cronbach's $\alpha=.80$) subscales. HADS-A (anxiety) and HADS-D (depression) were included as continuous sum scores in the regression models (7).

TAS-20 is a scale that investigates alexithymia. It is a Likert-type self-assessment scale that consists of three subscales with a total of twenty items. The subscale for difficulty recognizing emotions (TAS-1) is defined as difficulty identifying emotions and differentiating them from bodily sensations; the subscale for difficulty expressing feelings (TAS-2) is defined as hardness of transmitting emotions to others; while the subscale for extroverted thinking (TAS-3) is defined as the disability of introverted thinking and imagination power. High scores indicate a high level of alexithymia, while the cutoff value for TAS-20 is 51 or less, with 52–60 indicating possible alexithymia and a score of >61 confirming alexithymia (8).

Statistical Package for Social Science (IBM SPSS Statistics New York, USA) version 20.0 was used to perform statistical analyses. Descriptive statistics are reported as means $\pm$ SDs for continuous variables and as number and frequencies for binary and categorical variables. The normality of continuous variables was investigated using the Shapiro-Wilk test. Descriptive statistics are presented as mean and standard derivation for normally distributed variables and median (and minimum maximum) for non-normally distributed groups. Student t test was used. Non-parametric statistical methods were used for values with skewed distribution the comparison of 2 non-normally distributed groups, the Mann-Whitney U test was used. The Chi-square (χ^2) test was used for categorical variables and expressed as observation counts (and percentages). The logistic regression was used to analyze the alexithymia in chronic kidney disease. Variables were entered into a univariate (UV) logistic regression model. In addition, parameters that we thought would be significant such as age, gender, disease duration, anxiety and depression were included in the model. A multivariate (MV) logistic regression model was then constructed using an enter procedure among those candidate variables with the significance level $p<0,05$ was set as statistical significance.

RESULTS

A total of 111 patients (mean age 58.10 ± 13.48 years, 61% female) were included in the study, 72 (64.9%) of whom were CKD patients on hemodialysis and the remaining 39 CKD patients in the pre-dialysis stage. The control group included 33 subjects.

Table 1 represents the demographic and clinical data of the overall study population and the pre-dialysis (PG) and hemodialysis subgroups (HG).

Table 1. Demographic and clinical data

	Pre-dialysis group (n:39) Median, range	Hemodialysis group (n:72) Median, range	p value	Overall (n=111) Median, range
Female/Male (n)	17/22	34/38	0.512	51/60
Age (years)	56.77±2.182 (19-77)	58.82±1.584 (20-75)	0.496	55,27±2.085 (35-82)
Disease duration (month)	71.33±5.590 (12-154)	68.80±9.200 (4-360)	0.424	69.71±64.93 (4-360)
CKD ethology				
Hypertension (n)	10	33	0.037	43
Diabetes Mellitus (n)	12	19	0.623	30
Glomerulonephritis (n)	2	8	0.293	10
Polycystic kidney disease (n)	1	1	0.657	2
Others (n)	11	10	0,066	21
Literacy (n)	35	66	0.735	101
Education (n)			<0.024	
Illiterate (n)	5	6		11
Primary education (n)	9	38		47
Middle school (n)	12	10		22
High school (n)	9	9		18
University (n)	4	9		13
Alexithymia (n)	35	58	0.210	93
Possible alexithymia	16	29		45
Alexithymia	19	29		48
Total alexithymia score	60.82±1.295 (38-76)	58.26±0.981 (36-75)	0.118	53.00±10.592 (27-73)
Depression (n)	18	30	0.693	48
Depression score	7.54±0.698 (0-17)	6.80±0.511 (0-17)	0.443	7.09±0.710 (1-16)
Anxiety (n)	17	25	0.387	42
Anxiety score	7.51±0.868 (0-19)	6.21±0.522 (0-19)	0.234	6.70±0.716 (1-17)

P<0.05, CKD: Chronic kidney disease

The mean age of patients was 55.27±2.085 years. There was no significant difference between PG and HG according to mean ages (p: =.496)

Hypertension (43) and diabetes (30) were the most common etiology of chronic kidney disease in our patients.

Mean duration of hemodialysis of patients was 69.71±64.93 months. There wasn't statistically difference between two groups according to hemodialysis duration (p: 0.424).

Up to 83.9% of the patients were found to have alexithymia, while 60.6% of the control group had alexithymia. The mean TAS score of the patients was 57.75±9.209, average depression score according to HADS was 7.07±4.234, while anxiety score was 6.68±4.638. The prevalence of alexithymia in CDK patients was significantly higher than that in the control group (p=0.004), and comparing the pre-dialysis and control groups, the prevalence incidence of alexithymia was determined to be higher in the former than that in the control group (p=0.004). The prevalence of alexithymia in the HG was also found to

be higher than the control group (p=0.030). However, no statistically significant difference in the prevalence of alexithymia was detected between the HG and PG groups (p>0.05). Furthermore, there was no statistically significant difference between the TAS scores of the HG and those of the PG patients (p=0.118).

Table 2 shows the comparisons between the patients have alexithymia (AG) and patients don't have alexithymia (NAG). No difference was detected between the educational statuses of AG and NAG (p>0.05).

The TAS results of 40.45% of the CKD patients indicated possible alexithymia, while 43.45% of the patients were confirmed to have alexithymia.

Table 3 shows the logistic regression analysis made to predict alexithymia in CKD patients. The results show that increased prevalence of depression resulted in a 4.47-fold increase in the prevalence of alexithymia (p=0.035). However, no difference in the prevalence of alexithymia was detected based on the patients' age, sex, duration of disease, and treatment type (conservative or hemodialysis).

Table 2. Correlation between alexithymia and non-alexithymia group			
	Alexithymia Group (n:93)	Non alexithymia Group (n:18)	p value
Female/Male (n)	44/49	7/11	0.512
Age (years) (Median,Range)	58.12±12.49 (19-82)	55.00±15.34 (20-77)	0.496
Disease duration (month) (Median, Range)	72.78±68.91 (5-360)	54.17±36.55 (4-120)	0.424
Etiology			
Hypertension (n)	37	6	0.584
Diabetes Mellitus (n)	26	4	0.599
Glomerulonephritis (n)	8	2	0.744
Polycystic kidney disease (n)	1	1	0.194
Others (n)	16	5	0.305
Depression	45	3	0.012
Anxiety	39	3	0.040
Hemodialysis group (n:72)			
Kt/V (n)	42	8	0.266
URR (n)	48	12	0.790
Hemoglobin (g/dl)	10.47±1.23	11.34±1.28	0.049
Albumin	3.98±3.57	4.07±3.67	0.630
C-reactive protein (mg/L)	13.32±19.35	7.24±8.74	0.757
P<0.05 URR: Urea reduction ratio			

Table 3. Logistic regression analysis for factors associated with alexithymia, Model-B							
	B	S.E.	Wald	Exp (B)	Model B %95 CI		P
					Lower	Upper	
Gender	-0.321	0.626	0.262	0.726	0.213	2.477	0.609
Age	0.027	0.020	1.865	1.028	0.988	1.069	0.172
Duration of disease	0.005	0.006	0.738	1.005	0.994	1.016	0.390
Depression	1.499	0.713	4.423	4.477	1.107	18.101	0.035
Anxiety	1.104	0.760	2.108	3.015	0.680	13.378	0.147
Group	-0.824	0.650	1.608	0.439	0.439	0.123	0.205
Nagelkerke Model B: 0.218							

DISCUSSION

In this study, we found that patients with CKD had significantly higher scores for alexithymia, depression, and anxiety than those in the control group, and there was no statistically significant difference in terms of alexithymia development between the patients on hemodialysis and patients undergoing conservative therapy. Furthermore, no link was observed between the age of the patients and development of alexithymia. The results have also shown that depression was increased in CKD patients with alexithymia.

According to several studies prevalence of alexithymia is between 10%-23% in general population (9-11). In a study conducted with 300 healthy individuals, most of whom (77%) were university students and graduates in our country, it was reported that 20% of individuals showed alexithymic symptoms (12).

In our study, we found the prevalence of alexithymia in control group to be significantly higher than these studies. We think that this difference is related to the education levels, ethnic origins and socioeconomic conditions of the population participating in the studies and the time intervals in which the studies were conducted.

The prevalence of emotional disorders is higher in CKD patients compared to the general public due to restricted diet and physical activity, intensive medical treatments, and fear of death, and the emotional disorders and stress CKD patients suffer are major contributing factors to the development of alexithymia. This study has found that 13-83% of CKD patients undergoing hemodialysis suffer from alexithymia (13). These results are consistent with those from previous literature such as the study by Jardonova et al. (4) in which it was found that half of the patients on dialysis manifested alexithymia.

Lai et al. (14) reported that pre-dialysis CKD patients had a higher prevalence of alexithymia than that of dialysis patients, although the difference was not statistically significant, and was predicted to be due to the fact that the pre-dialysis patients did not want to face their feelings about being chronically ill as an escape mechanism, meanwhile, the dialysis patients could not ignore the reality of the situation, since they received invasive treatments. Similarly, the results from this study show that the pre-dialysis CKD patients had a higher prevalence of alexithymia than the control group; however, no statistically significant difference was observed in the prevalence of alexithymia between the pre-dialysis and hemodialysis patient groups.

Advanced age is related to higher grades of alexithymia in the general population, and a potential reason for the brain's frontal lobe's functional disruption.¹² Individuals over 65 years with no comorbidities or signs of dementia show significantly higher prevalence of alexithymia compared to younger individuals (15), and several studies have established a higher prevalence of alexithymia in HD patients above the age of 60 (16). Similar to the findings from this study, Pojatic et al. (17) did not observe a correlation between the age of hemodialysis patients and development of alexithymia. Therefore, it is possible that patients undergoing chronic hemodialysis develop high levels of alexithymia through other mechanisms, and alexithymia serves as a defense mechanism against physical stressors (18).

Although some studies have directly correlated the duration of dialysis with alexithymia score (19), we found no significant relationship between duration of dialysis and duration of disease and development of alexithymia, perhaps because the sample size was small and mean age of patients was <60 years.

Furthermore, anxiety and depression are seen in patients with chronic illnesses, and depression among CKD patients, including those not on hemodialysis, may cause rapid decline in physical health, resulting in adverse outcome (20). Anxiety in pre-dialysis CKD patients is associated with poor clinical outcome such as depression (21), and in the study by Duan et al. (22), and Wang et al. (23) no significant difference in depression traits across CKD stages was reported, whereas other studies reported that CKD patients in stages 4 and 5 were more likely to have depression than those in the early stages. From the present study, no significant differences in the development of anxiety and depression was observed between the pre-dialysis and hemodialysis groups. However, the patients who were alexithymic had increased depression and anxiety scores.

Only depression was determined as a risk factor for alexithymia in the multivariable regression analysis, and whereas older studies have reported negative correlations between depression and alexithymia, more recent studies that used the TAS-20 found positive correlations similar to those from this study (24). This difference may be due to the fact that the older studies utilized the MMPI alexithymia scale, which lacks certain psychometrics that TAS-20 includes.

The results showed a negative correlation between hemoglobin levels and alexithymia scores of CKD patients, and no correlations were detected between the development of alexithymia and high CRP, ferritin, and albumin levels, all of which increase morbidity in hemodialysis patients. Meanwhile, a statistically

significant negative correlation was found between development of alexithymia and hemoglobin levels among the hemodialysis patients. Although these findings were statistically significant, it does not suffice to claim that low hemoglobin levels increase the prevalence of alexithymia. A study conducted by Aktyz et al. (6) on 51 hemodialysis patients reported no correlation between hemoglobin levels and alexithymia development. Therefore, the relationship between alexithymia and hemoglobin levels in CKD patients should be further investigated using larger sample sizes for a more accurate claim.

One of the limitations of this study is the fact that it was not multicentric, and the pre-dialysis patients were not categorized into subgroups based on their CKD staging. Exclusion of peritoneal dialysis and renal transplant patients are also some of the limitations that should be mentioned.

Although the incidence alexithymia has been previously studied in CKD patients on hemodialysis, only few studies have been conducted on the prevalence of alexithymia in pre-dialysis CKD patients. Therefore, the results from the present study are highly valuable regardless of the limitations of the study. Furthermore, the fact that the pre-dialysis CKD patients also had increased alexithymia scores is of importance, since this affects the emotional state, treatment compliance, and disease progression of these patients.

CONCLUSION

The study results showed that the prevalence of alexithymia in CKD patients is higher than that in the control group; however, no difference in the prevalence of alexithymia was observed between hemodialysis and conservative treatments for CKD patients. Also, it was found that depression increased the prevalence of alexithymia in CKD patients, and that the prevalence of alexithymia also increased when the patients had a GFR of <60 mL/min/day.

The overall results of this study indicate that healthcare workers should be wary of patients' emotional states alongside their physical states while under their care, and that patients with chronic diseases such as CKD especially require close attention due to their increased depression, anxiety as well as incidence of alexithymia.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Ümraniye Training and Research Hospital Clinical Researches Ethics Committee (Date: 21.04.2022, Decision No: B.10.1.TKH.4.34. H.GPO.0.01/156).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

REFERENCES

1. Ammirati AL. Chronic kidney disease. *Rev Assoc Med Bras* 2020; 66: 53–9.
2. Agarwal AK, Ahmad S, Allon M. *Handbook of dialysis*; Wolters Kluwer Health: Philadelphia, PA, USA, 2015; ISBN 9781451144291.
3. Ibrahim S, El Salamony O. Depression quality life and malnutrition- inflammation scores in hemodialysis patients. *Am J.Nephrol* 2008; 28: 784–91.
4. Pop-Jordanova N, Polenakovic M. Alexithymia construct in dialysis patients. *BANTAO Journal* 2015; 12: 45–51.
5. Akyuz O, Parmaksiz E, Ardahanli I. Investigation of the relationship between Biochemical Parmeters, Alexithymia and Stress levels in hemodialysis patients. *South Clin IstEuras* 2021; 32: 13–8.
6. Christensen AJ, Ehlers SL. Psychological factors in end stage renal disease: An emerging context for behavioral medicine research. *J Consult Clin Psychol* 2002; 70: 712–24.
7. Herrmann C. International experiences with the hospital anxiety and depression scale-a review of validation data and clinical results. *J Psychosomatic Res* 1997; 42: 17–41.
8. Salbas E. The Twenty-Item Toronto Alexithymia Scale (TAS-20), 2016. Available at: <http://www.fronline.com/toronto-aleksitimiolecegi/>. Accessed May 20, 2017.
9. Mattila AK, Salminen JK, Nummi T, Joukamaa M. Age is strongly associated with alexithymia in the general population. *J Psychosomatic Research* 2006; 61: 629–35.
10. Salminen JK, Saarijärvi S, Äärelä E, Toikka T, Kauhanen J. Prevalence of alexithymia and its association with sociodemographic variables in the general population of Finland. *J Psychosomatic Research* 1999; 41: 75–82.
11. Loas G, Fremaux D, Otmani O, Verrier A. Prevalence of alexithymia in a general population. Study in 183 “normal” subjects and in 263 students. *Annales Medico-psychologiques* 1995; 153: 355–7.
12. Batıgün AD, Büyüksahin A. Alexithymia: Psychological Symptoms and Attachment Styles. *Klinik Psikiyatri* 2008; 11:105–14.
13. Pojatić Đ, Tolj I, Pezerović D, Degmečić D. Systematic review of alexithymia in the population of hemodialysis patients. *J Clin Med* 2021; 10: 28–62.
14. Lai C, Aceto P, Luciani M, et al. Emotional management and biological markers of dietetic regimen in chronic kidney disease patients. *Ren Fail* 2017; 39: 173–8.
15. Onor M, Trevisiol M, Spano M, Aguglia E, Paradiso S. Alexithymia and aging: a neuropsychological perspective. *J Nerv Ment Dis* 2013; 198: 891–5.
16. Fukunishi, I. Psychosomatic aspects of patients on hemodialysis. With special reference to aged patients. *Psychother Psychosom* 1989; 52: 51–7.
17. Pojatić Đ, Nikić D, Tolj I, Pezerović D, Šantić A, Degmečić D. Alexithymia, phosphorus levels, and sleep disorders in patients on hemodialysis. *J Clin Med* 2022; 11: 3218.
18. Besharat MA, Shahidi S. What is the relationship between alexithymia and ego defense styles? A correlational study with Iranian students. *Asian J. Psychiatry* 2011; 4: 145–9.
19. Cabras PL, Albanesi G, Calabresi M, Martinelli F. Chronic dialysis and forcing of the ability to fantasize. Evaluation of the alexithymic phenomenon in a group of dialyzed patients. *Riv Patol Nerv Ment* 1983; 104: 213–23.
20. Aggarwal HK, Jain D, Dabas G, Yadav RK. Prevalence of depression, anxiety and insomnia in chronic kidney disease patients and their relation with the demographic variables. *Pril* 2017; 38: 35–44.
21. Loosman WL, Rottier MA, Honig A, Siegert CEH. Association of depressive and anxiety symptoms with adverse events in Dutch chronic kidney disease patients: a prospective cohort study. *BMC Nephrol* 2015; 16: 155.
22. Duan D, Yang L, Zhang M, Song X, Ren W. Depression and associated factors in Chinese Patients with chronic kidney disease without dialysis: a cross-sectional study. *Front Public Health* 2021; 9: 605–51.
23. Wang X, Shen B, Zhaung X, Weng X. Investigating factor associated with depressive symptoms of chronic kidney disease in China with type 2 diabetes. *J Diabetes Res* 2017; 17: 698–97.
24. Kojima M, Hayano J, Suzuki S, et al. Depression, alexithymia and long-term mortality in chronic hemodialysis patients. *Psychother. Psychosom* 2010; 79: 303–11